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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/283,431	04/01/99	ZHOU W	475.08.423

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EXAMINER	
HICKEY,K	
ART UNIT	**PAPER NUMBER**
1635	5

DATE MAILED: 10/13/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)	
09/283431	Zhou et al	
Examiner	Group Art Unit	
Karen A Hickey	1635	5

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-3 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-3 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

DETAILED ACTION

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there are amino acid and nucleotide sequences disclosed in the drawings and the text of the specification which have not been submitted in computer readable format as required by the rules set forth in 37 CFR 1.821 through 1.825. Additionally, sequences should be assigned sequence ID numbers and should be identified using those numbers in the format SEQ ID NO: # when referred to in the specification, figure legends and claims.

A complete reply to this Office action must include compliance with this request.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 are drawn to an "improved" antisense oligonucleotide which contains one or more blocks of alternating phosphodiester and phosphorothioate bonds.

Claims 1-3 recite an improvement on an antisense molecule, without defining the scope of what antisense that includes, in terms of what was known in the art. In the case of a claim which admits to an improvement, such as a Jepson claim, an independent claim is required to include "a preamble comprising a general description of all the elements or steps of the claimed combination which are conventional or known" (see MPEP 1.75 (e)). Claims 1-3 recite an improvement, but do not provide a general description of the elements of the known antisense oligonucleotides which are being improved upon. Although the improvement is defined, the antisense oligonucleotide is not, therefore one skilled in the art would not know what antisense oligonucleotides are encompassed by these claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Arnold et al.

Claims 1 and 2 are drawn to an antisense oligonucleotide containing "POPS Blocks", wherein pops blocks are defined to be regions of alternating nucleoside phosphodiesters and

nucleoside phosphorothioates (see p6, lines 14-31). The pattern of phosphorothioate and phosphodiester bonds can be variable, but the ratio remains between 1:3 and 3:1. Additionally, the claims are drawn to oligonucleotides which contain "POPS Blocks" and are hybrid oligonucleotides, wherein hybrid is defined as an oligonucleotide containing deoxynucleotides flanked by ribonucleotides, 2'-substituted ribonucleotides (including 2'-OMethyl), or a combination thereof.

Arnold et al. teach antisense oligonucleotides which have a core of alternating phosphodiester and phosphorothioate bonds, flanked by regions of 2' O-methyl substituted bases (see p 85-88). Therefore, Arnold et al. anticipates claims 1 and 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Arnold et al. in view of Agrawal et al.

Claim 3 is drawn to an antisense oligonucleotide containing regions of alternating nucleoside phosphodiesters and nucleoside phosphorothioates and are inverted hybrid

oligonucleotides, wherein inverted hybrid is defined as an oligonucleotide with a core consisting of ribonucleotide or 2' substituted ribonucleotide bases flanked by deoxyribonucleotide bases.

Arnold et al. teach oligonucleotides with an alternating phosphodiester and phosphorothioate backbone to provide nuclease resistance (see p 9, lines 20-24 and p 11, line 29 and p 85-88) in chimeric and hybrid oligonucleotides. Arnold et al. do not teach making antisense oligonucleotides with an alternating phosphodiester and phosphorothioate backbone in an inverted chimeric hybrid.

Agrawal et al. teach making inverted hybrid oligonucleotides with chimeric backbones, throughout their disclosure and claims, because inverted hybrid oligonucleotides have fewer side effects relative to traditional phosphorothioate, hybrid or chimeric oligonucleotides (see abstract).

It would have been obvious to one skilled in the art at the time the invention was made to make an inverted hybrid antisense oligonucleotide with an alternating phosphorothioate and phosphodiester backbone to derive both the benefit of nuclease stability from the alternating backbone and reduced side effects from the inverted hybrid. From Arnold et al., one of ordinary skill in the art would have recognized that incorporation of an alternating phosphodiester and phosphorothioate backbone into any antisense oligonucleotide would have imparted greater stability against nucleases. Therefore, one of ordinary skill in the art would have expectated that incorporating an alternating phosphodiester and phosphorothioate backbone into the prior art inverted hybrid oligonucleotide taught by Agrawal would have imparted the benefit of nuclease stability, as taught by Arnold et al.

Any inquiry concerning this communication should be directed to Karen A. Hickey at telephone number (703)308-7523.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliot can be reached at (703) 308-4003. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Hickey
October 7, 1999